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10/717,559

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Hang-Ching Lin

LINH3023/EM

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12/10/2007

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EXAMINER

HUYNH, CARLIC K

ART UNIT

PAPER NUMBER

1617

MAIL DATE

DELIVERY MODE

12/10/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/717,559

Applicant(s)

LIN ET AL.

Examiner

Carlic K. Huynh

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1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on September 5, 2007 is acknowledged.

Status of the Claims

1. Claims 1-13 are pending in the application, with claims 1-5 and 14-23 having been cancelled, in an "Amendment – After Non-Final Rejection" filed on September 5, 2007.

Accordingly, claims 6-13 are being examined on the merits herein.

Response to Arguments

2. Applicants' amendments, see "Remarks" filed on September 5, 2007, with respect to "Objection to the Specification" (page 7) have been fully considered and are found persuasive. Applicants have amended the abstract by adding the word "the" prior to "human body". Thus the objection to the specification has been withdrawn in light of the amendments.

3. Applicants' arguments, see "Amendment-After Non-Final Rejection" filed on September 5, 2007, with respect to "Rejections under 35 U.S.C. § 112, 2nd paragraph" to claims 1-2 and 13 have been fully considered and are found persuasive. Claim 13 has been amended to correct the pentavalency of the carbon atoms at positions 8 and 9, which are no longer pentavalent. Furthermore, claims 1 and 2 have been cancelled. Thus, the Rejections under 35 U.S.C. § 112, 2nd paragraph to claims 1-2 and 13 have been withdrawn in light of the amendments.

4. Applicants' amendments, see "Amendment-After Non-Final Rejection" filed on September 5, 2007, with respect to "Rejections under 35 U.S.C. § 102(b)" to claims 1-5 have

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been fully considered and are persuasive. Claims 1-5 have been cancelled. Thus, the Rejections under 35 U.S.C. § 102(b) to claims 1-5 have been withdrawn in light of the amendments.

5. Applicants' amendments, see "Amendment-After Non-Final Rejection" filed on September 5, 2007, with respect to "Rejections under 35 U.S.C. § 102(e)" to claims 1-5 have been fully considered and are persuasive. Claims 1-5 have been cancelled. Thus, the Rejections under 35 U.S.C. § 102(e) to claims 1-5 have been withdrawn in light of the amendments.

6. Applicants' arguments, see "Amendment-After Non-Final Rejection" filed on September 5, 2007, with respect to "Rejections under 35 U.S.C. § 103" to claims 6-13 has been fully considered and are not persuasive. Applicants have argued Takahashi et al. (JP 8-119864) do not teach a lanostane of formula (I) that is substantially devoid of secolanostane. Applicants have also argued Tai et al. (Phytochemistry. 1995. Vol. 39, No. 5. pp. 1165-1169) do not teach a lanostane of formula (I) that is substantially devoid of secolanostane.

Regarding Takahashi et al., examiner maintains and argues that Takahashi et al. teach at least one compound having a lanostane skeleton or a 3,4-secolanostane skeleton (page 5, paragraph [0001]). Accordingly, Takahashi et al. do teach a compound having a lanostane skeleton of formula (I). Polyporenic acid C, pachymic acid, and dehydropachymic acid are all appropriate lanostane compounds of formula (I) (pages 11-12, paragraph [0011]). The extraction method of Takahashi et al. yielded 33 mg of polyporenic acid C, 500 mg of pachymic acid, and 100 mg of dehydropachymic acid, for a total of 633 mg in 86.4 g of extract or 0.7% of the extract. It would be obvious that the extract may contain 5 to 60% of a lanostane compound of formula (I) because the skilled artisan would know how to optimize the extraction process to yield the appropriate amount of lanostane compounds of formula (I).

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Regarding Tai et al., examiner maintains and argues that Tai et al. teach purification of compounds 1 and 2, both of which are lanostane compounds of formula (I). However, Tai et al. do not teach improving immunity using lanostane compounds of formula (I).

Moreover, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Furthermore, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Thus, the Rejections under 35 U.S.C. § 103 to claims 6-13 have been maintained.

7. Applicants' arguments, see "Amendment-After Non-Final Rejection" filed on September 5, 2007, with respect to "Rejections under 35 U.S.C. § 103" to claims 6-13 has been fully considered and are not persuasive. Applicants have argued that Babish et al. (US 2002/0068098) do not teach a Poria extract. Applicants have also argued that Cuellar et al. (Chemical and Pharmaceutical Bulletin. 1997. Vol. 45, No. 3. pp. 492-494) do not teach a lanostane compound of formula (I). Applicants have further argued that Tai et al. (Phytochemistry. 1995. Vol. 39, No. 5. pp. 1165-1169) do not teach a lanostane of formula (I) that is substantially devoid of secolanostane. Regarding Babish et al., examiner maintains and argues that Babish et al. teach triterpenes, which may be pachymic acid, a lanostane compound of formula (I) and accordingly, Babish et al. do teach a lanostane compound of formula (I), regardless on the source (Poria

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extract) of the lanostane compound of formula (I). Regarding Cuellar et al., examiner maintains and argues that Cuellar et al. teach isolation of compound 1, or pachymic acid, which is a lanostane compound of formula (I). Regarding Tai et al., examiner maintains and argues that Tai et al. teach purification of compounds 1 and 2, both of which are lanostane compounds of formula (I). Moreover, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Furthermore, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Thus, the Rejections under 35 U.S.C. § 103 to claims 6-13 remain rejected as being unpatentable over Babish et al. in view of Cuellar et al. and Tai et al.

8. Applicants' arguments with respect to claims 1-13 have been considered but are moot in view of the new ground(s) of rejection. The following new ground(s) of rejection to amended claims 6-13 are used herewith.

Claims 6-13 are drawn to a Poria extract and thus intended use is not given any patentable weight. The recitation "enhancing immunity" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a

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structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi et al. (JP 8-119864) in view of Tai et al. (Phytochemistry. 1995. Vol. 39, No. 5. pp. 1165-1169).

Note a full translation of the Japanese Patent will be used for citation purposes and is provided herewith.

Takahashi et al. teach the compound of formula 13 and formula 14, which reads on the elected species in instant claim 2 where R₂ is CH₃COO (paragraph [0007]). The compound of formula 13 is 10% by weight of a 200 mg tablet (paragraph [0049]). The compound of formula 13 is administered orally to humans (paragraph [0036]).

Takahashi et al. further teach the extraction of the compound of formula 13 and the compound of formula 14, which reads on the elected species in instant claim 13 where R₂ is CH₃COO (paragraph [0011]). Poria is extracted with methanol and the extract contains 0.6% lanostane compounds of formula (I) (paragraph [0011]). The resulting liquid extract was

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concentrated with reduced pressure, subjected to silica gel column chromatography, and eluted with chloroform and methanol (50:1) (paragraph [0011]).

Takahashi et al. do not teach the step of concentrating the eluate to form a concentrated eluate with thin layer chromatography (TLC) in the extraction of *Poria cocos*.

Tai et al. teach extraction of various lanostane compounds of formula (I) (page 1168). The extraction involves exposing the sclerotia of *Poria cocos* to methanol (page 1168). The liquid extract was dried and concentrated with Et₂O (pages 1168-1169). The resultant concentrated extract was introduced into a silica gel column with CHCl₃ and MeOH-CHCl₃ gradient mixtures (page 1169). The extract was rechromatographed on a silica gel column with MeOH-CHCl₃ (page 1169). Purification was performed using TLC with MeOH-CHCl₃ (1:199) (page 1169).

To a person of skill in the art at the time of the invention, it would have been obvious to employ the lanostane (I) compounds of Takahashi et al. to undergo purification with TLC because the lanostane compounds of Tai et al. have undergone purification with TLC and according to Tai et al., the extraction of lanostane compounds from *Poria cocos* includes the step of purification with TLC.

The motivation to combine the compounds of Tai et al. to the compounds of Takahashi et al. is that the compounds of Tai et al. are lanostane compounds that have undergone purification with TLC.

Regarding 10-20% of the lanostane (I) as recited in instant claims 6 and 12, Takahashi et al. teach *Poria cocos* extracts containing about 0.7% by weight of lanostane (I) compounds (paragraph [0011]), which meets the limitations of the instant claims. It is considered that one of

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ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the weight of the lanostane (I) compounds provided in a composition, according to the guidance set forth in Takahashi et al., to provide an extract having the desired percentage weight of the lanostane (I) compounds in *Poria cocos* extracts. It is noted that “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

Regarding the chromatographic value, Rf, and the mixed solvent as recited in instant claim 8, it would be obvious to one skilled in the art at the time of the invention to change the solvent used and thus change the Rf value in order to meet the limitations of the claim. Solvents are routinely changed due to the polarity of the compounds to extract and the availability of the solvent. Because the solvents can be changed, the resulting Rf will also change.

Regarding 95% ethanol as recited in instant claim 9, Takahashi et al. teach extraction of lanostane (I) compounds with ethanol (paragraph [0011]) and Tai et al. teach extraction of lanostane (I) compounds with methanol (page 1168), which meets the limitations of the instant claims. It is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the percentage of methanol provided in a composition, according to the guidance set forth in Takahashi et al. and Tai et al., to provide a composition having the desired percentage of methanol. It is noted that “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

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Regarding the two-phase solvent as recited in instant claim 10 and the mixed solvent as recited in instant claim 11, it would be obvious to one skilled in the art at the time of the invention to change the solvent used in order to meet the limitations of the claims. Solvents are routinely changed due to the polarity of the compounds to extract and the availability of the solvent.

10. Claims 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babish et al. (US 2002/0068098) in view of Cuellar et al. (Chemical and Pharmaceutical Bulletin. 1997. Vol. 45, No. 3. pp. 492-494) and Tai et al. (Phytochemistry. 1995. Vol. 39, No. 5. pp. 1165-1169).

Babish et al. teach a composition comprising pachymic acid, a triterpene, which reads on the elected species in instant claim 2 where R_2 is CH_3COO (page 3, Table 1). The composition contains preferably greater than 50% triterpene by weight (page 5, paragraph [0038]). The composition is given in capsule or tablet form to an adult human (page 5, paragraph [0045]).

Babish et al. do not teach an extraction method for a lanostane of formula (I), the step of eluting the silica gel column with an eluent having low polarity, and the step of concentrating the eluate.

Cuellar et al. teach extraction of pachymic acid from *Poria cocos* (page 494). The extraction involves, first, extracting metabolites from the sclerotium of *Poria cocos* with 50% aqueous ethanol (page 494). The extract was then concentrated with reduced pressure (page 494). The resultant concentrated extract was introduced into a silica gel column with a mixture of $\text{CHCl}_3/\text{EtOAc}$ to yield pachymic acid (page 494). Identification of pachymic acid was performed with ^3H - and ^{13}C -NMR spectral analysis (page 494). Moreover, Cuellar et al. teach that Hoelen or *Poria cocos* extract has a remarkable inhibitory effect on the secretion of the

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cytokines IL-1 β , IL-6, TNF- α , and GM-CSF as well as having a protective effect on stress-induced ulcers (page 492). Thus it would be obvious that the lanostane compounds of formula (I) may be used to enhancing immunity in mammals.

Tai et al. teach extraction of various lanostane compounds of formula (I) (page 1168). The extraction involves exposing the sclerotia of *Poria cocos* to methanol (page 1168). The liquid extract was dried and concentrated with Et₂O (pages 1168-1169). The resultant concentrated extract was introduced into a silica gel column with CHCl₃ and MeOH-CHCl₃ gradient mixtures (page 1169). The extract was rechromatographed on a silica gel column with MeOH-CHCl₃ (page 1169). Purification was performed using TLC with MeOH-CHCl₃ (1:199) (page 1169).

To a person of skill in the art at the time of the invention, it would have been obvious to employ the lanostane (I) compounds of Babish et al. to undergo extraction from *Poria cocos* because the lanostane (I) compounds of Cuellar et al. and Tai et al. have undergone extraction from *Poria cocos* and according to Cuellar et al. and Tai et al., lanostane (I) compounds can be extracted from *Poria cocos*.

The motivation to combine the compounds of Cuellar et al. and Tai et al. to the compounds of Babish et al. is that the compounds of Cuellar et al. Tai et al. are lanostane (I) compounds that have been extracted from *Poria cocos*.

Regarding 10-20% of the lanostane (I) as recited in instant claims 6 and 12, Cuellar et al. teach *Poria cocos* extracts containing about 1.3% by weight of lanostane (I) compounds, which meets the limitations of the instant claims (page 494). It is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or

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optimize the weight of the lanostane (I) compounds provided in a composition, according to the guidance set forth in Cuellar et al., to provide an extract having the desired percentage weight of the lanostane (I) compounds in *Poria cocos* extracts. It is noted that “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

Regarding the chromatographic value, Rf, and the mixed solvent as recited in instant claim 8, it would be obvious to one skilled in the art at the time of the invention to change the solvent used and thus change the Rf value in order to meet the limitations of the claim. Solvents are routinely changed due to the polarity of the compounds to extract and the availability of the solvent. Because the solvents can be changed, the resulting Rf will also change.

Regarding 95% ethanol as recited in instant claim 9, Tai et al. teach extraction of lanostane (I) compounds with methanol, which meets the limitations of the instant claims (page 1168). It is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the percentage of methanol provided in a composition, according to the guidance set forth in Tai et al., to provide a composition having the desired percentage of methanol. It is noted that “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

Regarding the two-phase solvent as recited in instant claim 10 and the mixed solvent as recited in instant claim 11, it would be obvious to one skilled in the art at the time of the invention to change the solvent used in order to meet the limitations of the claims. Solvents are

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routinely changed due to the polarity of the compounds to extract and the availability of the solvent.

Conclusion

11. No claims are allowable.
12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

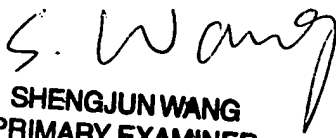
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ckh


SHENGJUN WANG
PRIMARY EXAMINER